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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/398,405	09/16/1999	JOHN C. SALERNO	JCS96-01Z	1062

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EXAMINER	
CANELLA, KAREN A	
ART UNIT	**PAPER NUMBER**
1642	20

DATE MAILED: 07/08/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/398,405	Applicant(s) Salerno
	Examiner Karen Canella	Art Unit 1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3 months* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-59* is/are pending in the application.

4a) Of the above, claim(s) *1-30, 34-47, and 51-59* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *31-33 and 48-50* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. After review and reconsideration, the finality of the Office action of Paper No. 16 is withdrawn.

2. Claims 32 and 49 have been amended. Claims 1-59 are pending. Claims 1-30, 34-47 and 51-59 remain withdrawn from consideration. Claims 31-33 and 48-50 are under consideration.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

4. The specification is objected to for not having an updated cross reference to the prior application. The specification should be amended to reflect that application 08/ 679,006 is now U.S. 6,150,500.

5. Claims 31, 33, 48 and 50 are objected to, as well as page 15, lines 15 and 16 of the specification, for not complying with 1.821(d) of the Sequence Rules and Regulations. When the specification or claims of a patent application discusses a sequence listing that is set forth in the "Sequence Listing" in accordance with paragraph (c) of the Sequence Rules and Regulations, reference must be made to the sequence by use of the assigned identifier, in the text of the description or claims of the patent application. Amino acids 590-650 of endothelial nitric oxide synthase are identified in the specification as SEQ ID NO:1. Amino acids 820-880 of neuronal nitric oxide synthase are identified in the specification as SEQ ID NO:2. Appropriate correction is required.

6. Claims 31, 33, 48 and 50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which

applicant regards as the invention. The claims are rendered vague and indefinite on the reliance of the phrase "amino acids 590-650 of endothelial nitric oxide synthase" and "amino acids 820-880 of neuronal nitric oxide synthase" as the only means for identifying the region of nitric oxide synthase on which the instant methods claims depend. Without a sequence identifier, the recited amino acid residues can read on regions of nitric oxide synthase in non-human homologs of NOS wherein said non-human homologue would be of a differing length and therefore the location of the recited residues would not correspond to the region of NOS which is responsible for auto-inhibition. Amendment of the claims to incorporate a sequence identifier for the recited amino acid residues would overcome this rejection.

7. Claims 32 48, 49 and 50 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of activating endothelial nitric oxide synthase and a method of treating a disease due to the lack of production of endothelial nitric oxide synthase in a mammal, both methods comprising the administration of SEQ ID NO: 6 or SEQ ID NO:7 and methods of treating a disease caused by underproduction of nitric oxide by endothelial or neuronal nitric oxide synthase, does not reasonably provide enablement for a method of activating endothelial nitric oxide synthase or a method of treating a disease modulated by production of endothelial nitric oxide synthase in a mammal, both methods comprising the administration of SEQ ID NO:4, 5, 8 or 9, or a method of treating a disease caused by the overproduction of nitric oxide by endothelial nitric oxide synthase or neuronal nitric oxide synthase. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

(A) As drawn to methods using SEQ ID NO:4, 5, 8 and 9 to activate eNOS

Claims 32 and 49 are drawn to method of activating endothelial nitric oxide synthase and methods of treating a disease modulated by production of nitric oxide by endothelial nitric oxide

synthase. The specification states on page 4 line 24 to page 5, line 2 that the object of the invention was to identify agents which act on specific isoforms of NOS. The specification teaches on page 15, lines 10-19 that the peptides corresponding to SEQ ID NO:6 and 7 interact with the regulatory region of eNOS; the peptides corresponding to SEQ ID NO:8 and 9 interact with the regulatory region of nNOS and the peptides of SEQ ID NO:4 and 5 interact with the regulatory region of iNOS. It is noted that claims 32 and 49 specifically state endothelial nitric oxide synthase. Given the teachings of the specification, one of skill in the art would not expect SEQ ID NO:4, 5, 8 or 9 to interact with the regulatory region of the endothelial isoform of NOS.
(B)As drawn to methods of treating a disease caused by the overproduction of nitric oxide

Claims 48, 49 and 50 when given the broadest reasonable interpretation read on diseases modulated by the overproduction as well as underproduction of nitric oxide by endothelial and neuronal NOS. The specification does not teach how to use any of the recited SEQ ID NO to decrease the activity of eNOS and therefore be useful in treating a disease caused by overproduction of eNOS. The MPEP (2164.01(b)) states that:

> As long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. 112 is satisfied. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

However in the instant case claims drawn to a "disease modulated by nitric oxide" read on diseases caused by overproduction as well as by under production of nitric oxide. Therefore, the specification has not enabled the broad scope of the claims.

8. All other rejections as set forth in Paper No. 16 are withdrawn.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Canella whose telephone number is (703) 308-8362. The examiner can normally be reached on Monday through Friday from 8:30 am to 6:00 pm. A message may

be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Karen A. Canella, Ph.D.

Patent Examiner, Group 1642

July 3, 2003